REMARKS

Applicants respectfully request entry of amendments to claim 22. Support for the amendments can be found throughout the specification and the originally filed claims and therefore, do not add new matter.

Applicants submit that pending claims 1, 10, 13, 15, 16, 22, 23, 25-29, 32, and 35-37 are in condition for allowance and respectfully request that the claims as amended be entered.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 22, 23, 25-39, 32 and 35-37 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants have amended claim 22 to remove the language concerning "media containing less than 15% serum" thereby rendering the rejection moot. In light of the amendment, withdrawal of the rejection of claims under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. §103(a)

Applicants respectfully traverse the rejection of claims 1, 10, 13, 15 and 16 under 35 U.S.C. §103(a) as allegedly being unpatentable over Hogan (U.S. Pat. No. 5,453,357; hereinafter, "Hogan" or "the Hogan patent") in view of Shamblott, et al. (1998, PNAS, pp 13726-31, hereinafter, "Shamblott").

The recent U.S. Supreme Court decision in the *KSR International v. Teleflex, Inc.* (127 S.Ct. 1727, 82 USPQ 2d. 1385 (2007)), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references. Applicants respectfully submit that the criteria for establishing a *prima facie* case of obviousness have not been satisfied.

The claims recite a human embryoid body derived (EBD) cell characterized by forming disaggregated single cells upon dissociation from embryoid bodies (EB) and adhering to defined extracellular matrix components lacking a feeder layer and lacking leukemia inhibitory factor; and having the ability to be maintained in culture on the defined extracellular matrix components in the absence of a feeder layer for at least thirty population doublings without being immortal under such conditions. Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in part, that "Hogan teaches mouse embryoid body cells isolated from mouse embryoid bodies (EB's), rounded colonies of densely packed ES-like cells, produced by the culture of mouse primordial germ cells" and "Shamblott teaches embryoid bodies (EB's) produced from human primordial germ cells (hPGC's)." (Office Action, page 3-4.) The Office Action also alleges that "the ordinary artisan at the time of filing would have reasonably expected the physiological characteristics to be the same for the claimed cells and those of Hogan even given species differences. Thus, the cells of Hogan in view of Shamblott undergo at least 30 or at least 60 population doublings, proliferate under conditions nonpermissive for the proliferation of human EG cells, proliferate under culture conditions lacking LIF, a fibroblast feeder layer, or both, and transfectable with a retrovirus, lentivirus or both. There is no evidence to the contrary on the record." (Office Action, page 4.)

Applicants continue to submit that the Examiner has mischaracterized the teachings of the Hogan. In contrast to the Examiner's assertion that "Hogan teaches mouse embryoid body cells...." and Hogan teaches "picking of single clones of EB-derived mouse cells..." (page 3 of Office Action), Hogan does not provide any EB-derived cells at all. Hogan describes in column 6, lines 19-50, not EB-derived cells, but rather cells that are derived from embryos and are referred to as primordial Germ Cells (GCs). GCs, in contrast to Applicant's EB-derived cells, require a feeder layer for growth. Hogan's GC cells, in contrast to Applicant's EB-derived cells can GIVE RISE to embryoid bodies but they are CELLS DERIVED from embryoid bodies as claimed in the present invention. Such GC cells of Hogan are pluripotent cells that under certain conditions, can differentiate INTO embryoid bodies, from which Applicants' cells could then be

derived. However, Hogan not only does not teach cells derived from embryoid bodies, they do not teach the differentiation of GC cells into embryoid bodies. At the time Hogan was filed in 1992, the stem cell field was quite immature. It appears that the Examiner is impermissibly using hindsight given the state of the stem cell field today, in assuming what Hogan was culturing and what their intent was in preparing certain GC cell preparations.

Further, for the sake of argument, even if Hogan had intended or described cells further derived from the mouse embryoid bodies, it would NOT provide the human cells of the claimed invention. Mouse EBD cells have very limited capacity for proliferation in culture if they are not immortalized. In sharp contrast, Applicant's human EBD cells are capable of long periods of cell proliferation and passages for years IN THE ABSENCE OF IMMORTALIZATION.

Shamblott describes the derivation of pluripotent stem cells from GERM CELLS, and not from embryoid bodies. The mouse GERM CELLS of Hogan and the human GERM CELLS of Shamblott were cultured in the presence of a fibroblast feeder layer and leukemia inhibitory factor (LIF). All of the cells described in Hogan and Shamblott would not proliferate in the absence of a fibroblast feeder layer, LIF, or both. The combination of the germ cells taught in Hogan and the germ cells taught in Shamblott, both of which require feeder layers for growth, cannot render a human cell derived from an EB that does not require LIF or a feeder layer for proliferation, obvious in any way. The human primordial germ cells of Shamblott were grown for 20-25 doublings on a fiberblast feeder layer, but again, these are germ cells and not embryoid body derived cells. Shamblottt mentions production of EBs from the PGCs but there is no suggestion that such cells should be cultured in the absence of feeder layers and/or LIF.

Since Hogan is silent as to any reason, desire or purpose in obtaining cells from a mouse or embryoid body, and Shamblott similarly teaches germ cells and not cells derived from an EB, let alone cells that require no feeder layer and LIF, one of skill in the art would have no motivation to combine the references to arrive at Applicants' invention and even if they did, they would not end up with the claimed Embryoid Body derived cells. Further, since they do not arrive at EBD cells, the combination of Hogan and Shamblott cannot render obvious the claims

of the application, in which the EBD cells are maintained in culture in the absence of a feeder layer (Hogan requires a feeder layer so even if they use HUMAN GCs, they would not arrive at Applicants' cells which do NOT require a feeder layer) and lacking leukemia inhibitory factor for at least thirty population doublings without being immortal.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed and no motivation to make the cells as claimed, there can be no *prima facie* case for obviousness exists. Further, there is no teaching or suggestion of all of the recited claim limitations. Accordingly, withdrawal of rejection of claims 1, 10, 13, 15 and 16 under 35 U.S.C. §103 is respectfully requested.

CONCLUSION

Applicants submit that pending claims 1, 10, 13, 15, 16, 22, 23, 25-29, 32, and 35-37 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

Please charge Deposit Account No. 07-1896 in the amount of $65.00 to cover a One-Month Petition for Extension of Time fee. The Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

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